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## Review

# Bio-environmental factors associated with myopia: An updated review<sup>☆</sup>

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### ABSTRACT

Experimental studies in animals, as well as observational and intervention studies in humans, seem to support the premise that the development of juvenile myopia is promoted by a combination of the effect of genetic and environmental factors, with a complex interaction between them. The very rapid increase in myopia rates in some parts of the world, such as Southeast Asia, supports a significant environmental effect. Several lines of evidence suggest that humans might respond to various external factors, such as increased activity in near vision, increased educational pressure, decreased exposure to sunlight outdoors, dietary changes (including increased intake of carbohydrates), as well as low light levels indoors. All these factors could be associated with a higher prevalence of myopia.

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### Los factores bioambientales asociados a la miopía: una revisión actualizada

### RESUMEN

Estudios experimentales en animales, así como observacionales y de intervención en humanos parecen apoyar la premisa de que el desarrollo de la miopía juvenil es promovido por una combinación del efecto de factores genéticos y ambientales, con una compleja interacción entre ellos. El muy rápido incremento de las tasas de miopía en algunas partes

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Trabajo en visión próxima y miopía  
Prevención de la miopía  
Exposición a la luz ambiental y miopía

del mundo, como el sudeste asiático, apoyan un efecto ambiental significativo. Diversas evidencias señalan que los seres humanos podrían responder a diversos factores externos, como el incremento de las actividades en visión próxima, el aumento de la presión educativa, la disminución de la exposición a la luz solar al aire libre, los cambios dietéticos (incluyendo el incremento de la ingesta de hidratos de carbono) y la baja iluminación en interiores, y que esto se podría asociar con una mayor prevalencia de miopía.

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## Introduction

Myopia is the most common refractive error worldwide. In 2011, it was estimated that 1.5 billion people were myopic, that is 23% of the world population, and it is expected that by 2020 this population will increase to 2.5 billion.<sup>1,2</sup> Since the late 1950s, importance genetic factors have been identified and estimations regarding inheritance, i.e., the proportion of phenotypic variation attributable to genetic variation due to refraction defects in twins is in the range of 75–90%.<sup>3–7</sup> Familial studies have generally produced estimations between 15 and 70%.<sup>7</sup> However, as members of a family frequently share a common environment, said inheritance calculations could be overestimated.<sup>7–9</sup> On the other hand, the identification of over 40 genetic loci associated to the appearance of myopia supports the genetic contribution to said disease.<sup>6,7,10–12</sup> In addition, an important predictor of myopia is myopia history in parents<sup>8,13–20</sup> (Jones LA, Sinnott L, GL Mitchell, et al. *How well do parental history and near sighted work predict myopia?* E-Abstract # 5452 ARVO, 2006). In a cohort study in Singapore on myopia risk factors (*Singapore cohort study of the risk factors for myopia*), Saw et al. found that children in school age with both parents being myopic had 1.6 times greater risk of being myopic than children without myopic parents.<sup>7,8,13,21,22</sup> In accordance with the recently published results of the *Growing up in Singapore toward healthy outcomes* study, Chua et al. pointed out that genetic factors could have a greater contribution to the early development of refraction error than environmental factors. In multivariate regression models, 3-year-old children with 2 myopic parents had higher probabilities of higher myopic spherical equivalents, longer axial length and greater propensity to myopia than children whose parents were not myopic.<sup>23</sup> However, other researchers explain that, even though said correlations are consistent with the idea of a genetic background for myopia, this background is not definitively established because, as mentioned above, parents and children also share environmental factors.<sup>9</sup> In addition, the influence of parental myopia in refractive error of school children and teenagers is not a universal finding. In 2004, Quek et al. reported in Singapore the absence of a statistically significant difference in the incidence of myopia between students aged 15–19 in accordance with the myopic history of their parents. However, they recognized that a shortcoming of this study was that the parental refractive state was established by interviewing the teenagers instead of their parents.<sup>24</sup> In a study

covering three generations of children in Hong Kong and northern China, Wu and Edwards found that the influence of parental history (at least one of the parents being myopic) in the probabilities of having myopia was greater in the second generation, i.e., in the generation of parents, than in the 3<sup>rd</sup> generation, i.e., the generation of the children. This finding supports greater effect of environmental vis-à-vis inheritance factors.<sup>9,20</sup>

Current evidence, including experimental studies, seems to support the premise that the development of juvenile myopia is driven both by genetic and environmental factors.<sup>8,17,21,25–27</sup> (Guggenheim JA. *Genetic susceptibility to myopia induced by the visual environment*. E-Abstract # 5243 ARVO, 2015). However, the mechanisms through which the genes identified as responsible for experimental myopia determine the appearance of refractive error are yet to be defined.<sup>17,25,28</sup> At present, as stated by Mutti et al. in their classic 1996 study (a statement that was apparently supported by research results in the past 20 years), in the debates between nature and environment which traditionally had opposite positions, the main question nowadays seems to have changed to what is the weight of these factors in the appearance of myopia.<sup>29</sup> In addition, as indicated by Morgan and Rose in their influential paper published in 2005, high inheritability does not establish any limit in the possibilities of environmentally induced change. At the time, said authors indicated that the concept that Eastern Asian populations had an intrinsically higher prevalence of myopia had the counter argument of the low prevalence reported in rural areas of some countries of the region as well as the high prevalence of myopia reported for other ethnic groups (such as Indians having different genetic information) that migrated to Southeast Asia.<sup>9,30–33</sup> Examples of low prevalence in Asian population groups include the report by Chang et al., who referred to a study carried out by Chen in Taiwanese students of non-aboriginal ethnicity carried out in the 80s, which found only 9.7% of prevalence of myopia.<sup>32</sup> Also in Taiwan in the decade of the 80s, Lin et al. found 20% myopia rate among native schoolchildren.<sup>31</sup> More recent findings in China and Singapore also seem to support that Southeast Asian people need not have a significantly higher and clear genetic predisposition to be myopic than other ethnic groups, as low prevalence estimates have also been reported in some population groups of said countries.<sup>34–37</sup> In addition, the premise that the genetic basis of Southeast Asians could make some more susceptible to risk factors does not seem to hold in the light of the findings of a

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